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SYSTEMATIC REVIEW

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Dynamic Measures of Fluid Responsiveness to Guide Resuscitation in Patients With Sepsis and Septic Shock: A Systematic Review and Meta-Analysis

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OBJECTIVE: To determine the impact of using dynamic measures of fluid responsiveness in guiding the resuscitation of adult patients with sepsis and septic shock.

DATA SOURCE: We searched MEDLINE, Embase, and unpublished sources from inception to February 3, 2025.

STUDY SELECTION: We included randomized controlled trials (RCTs) that evaluated the use of dynamic measures of fluid responsiveness to guide resuscitation compared with any other method in patients with sepsis and septic shock.

DATA EXTRACTION: We collected data regarding study and patient characteristics, definitions of fluid responsiveness, modality for assessing fluid responsiveness, and outcome data. We performed a random-effects meta-analysis and rated the certainty of the evidence using the Grading of Recommendations Assessment, Development, and Evaluation framework.

DATA SYNTHESIS: We included nine eligible RCTs ($n = 698$ patients). The use of dynamic measures of fluid responsiveness to guide IV fluid (IVF) administration of patients with septic shock probably reduces 28-day mortality (relative risk] 0.61; 95% CI, 0.42–0.90, moderate certainty), may reduce the risk of acute kidney injury (AKI) (RR 0.66; 95% CI, 0.44–0.98, low certainty), and cumulative fluid balance on day 3 (mean difference −1.57L; 95% CI, −2.44 L to −0.69 L, low certainty). The use of dynamic measures of fluid responsiveness has an uncertain effect on ICU mortality, ICU and hospital length of stay, need for and duration of mechanical ventilation, need for renal replacement therapy, vasoactive medication administration, duration of vasopressor use, and IVF administration on day 1.

CONCLUSIONS: In adult patients with sepsis and septic shock, using dynamic measures of fluid responsiveness may improve survival and reduce the risk of AKI. Future studies should evaluate the impact of this intervention on other important clinical outcomes and determine the comparative efficacy of specific modalities for assessing fluid responsiveness.

KEYWORDS: critical care; fluid responsiveness; hemodynamics; sepsis; shock

Despite advances in critical care medicine, septic shock remains a leading cause of ICU admissions and is associated with mortality rates as high as 50% (1). A cornerstone of early management is the administration of IV fluids (IVF) to augment preload, increase cardiac output, and improve tissue perfusion.

Determining the optimal volume of IVF for patients with sepsis and septic shock remains challenging for clinicians. Although clinical practice guidelines

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KEY POINTS

Question: Does using dynamic measures of fluid responsiveness impact outcomes in adult patients with sepsis or septic shock?

Findings: Using dynamic measures of fluid responsiveness probably reduces 28-day mortality, and the risk of acute kidney injury, and may reduce cumulative fluid balance by day 3. However, their effects on ICU mortality, ICU and hospital length of stay, and use of organ-sustaining therapies remain uncertain.

Meaning: Using dynamic measures of fluid responsiveness may improve survival in patients with sepsis and septic shock, but we require further studies to compare the efficacy of different modalities for assessing fluid responsiveness and evaluate their impact on other important clinical outcomes.

recommend an initial bolus of 30 cc/kg of IVF, they make no clear recommendation on the optimal fluid resuscitation strategy after the initial bolus (2). Clinicians need reliable tools to optimize preload while preventing complications of excessive IVF administration (3). However, static measures of volume status—such as heart rate, systolic blood pressure, and central venous pressure (CVP)—offer limited utility for guiding fluid therapy. CVP, in particular, correlates poorly with intravascular volume and does not reliably predict fluid responsiveness (4).

The 2021 Surviving Sepsis Campaign Guidelines recommend using dynamic measures of fluid responsiveness as tools to evaluate whether patients will benefit from additional IVF administration. These measures rely on preload-modifying techniques, such as the passive leg raise test, followed by assessments of cardiac output changes using pulse pressure variation and stroke volume variation as surrogate measures. By identifying patients whose cardiac output increases after IVF administration, clinicians can tailor fluid resuscitation to improve perfusion while preventing fluid overload. However, the supporting evidence remains of low quality and is primarily extrapolated from surgical populations (2). Although a meta-analysis of surgical studies suggests potential benefits (5), a meta-analysis in septic shock patients was inconclusive (3). A Grading of Recommendations Assessment, Development, and Evaluation (GRADE) assessment of the evidence has also yet to be performed.

In light of several recent clinical trials evaluating the efficacy of using dynamic measures of fluid responsiveness in patients with sepsis and septic shock (6–8), we aim to conduct a comprehensive evidence synthesis and GRADE-based evaluation. Our objective was to inform evidence-based fluid resuscitation strategies in sepsis and identify key areas for future research.

MATERIALS AND METHODS

We report this review following the Cochrane Handbook for Systematic Reviews and Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines (www.prisma-statement.org). We registered the protocol before abstract and full-text screening (PROSPERO ID: CRD42024564809).

Search Question, Patient Population, and Eligibility Criteria

This review sought to answer the question: In adults with sepsis and septic shock, does the use of dynamic measures of fluid responsiveness, compared with no use of dynamic measures of fluid responsiveness, improve patient-important outcomes (e.g., 28-d mortality, length of ICU stay) and impact the use of resuscitative therapies (e.g., IVF, fluid balance, vasopressor use). We included studies enrolling adults (18 yr or older) who met either Sepsis II or III criteria or explicitly reported patients meeting some pre-set criteria for sepsis or septic shock. We included randomized controlled trials (RCTs) with at least one study arm examining IVF administration guided by dynamic measures of fluid responsiveness. We defined dynamic measures of fluid responsiveness as physiologic parameters or techniques that assess whether variations in preload predict whether a patient's cardiac output will increase in response to fluid administration. These measures include but are not limited to performing a passive leg raise test, pulse pressure variation, stroke volume variation, systolic pressure variation, inferior vena cava distensibility or collapsibility, end-expiratory occlusion test, mini-fluid challenge, and global end-diastolic index. In the comparator arm, methods to

guide fluid resuscitation include, but are not limited to clinical assessment and/or early goal-directed therapy. To maintain a pragmatic and inclusive approach, we placed no restrictions on the hemodynamic monitoring tools used to measure these physiologic parameters. We included studies using noninvasive cardiac output monitors, transpulmonary thermodilution devices, bioreactance, pulse contour analysis systems, point-of-care ultrasound, and esophageal Doppler. We screened the references of review articles to identify additional eligible studies.

We assessed both patient-important and clinical outcomes, including 28-day mortality, ICU mortality, ICU and hospital length of stay, the use and duration of invasive mechanical ventilation (MV) and renal replacement therapy (RRT), as well as the occurence of acute kidney injury (AKI) as defined by each individual study. In addition, we evaluated whether using dynamic measures of fluid responsiveness influenced resuscitative interventions—specifically, the use of vasopressors (e.g., norepinephrine), inotropes (e.g., dobutamine), fluid administration on day 1, and cumulative fluid balance on day 3 following randomization.

Search Strategy

Guided by a health information specialist, we applied the Cochrane highly sensitive strategy for identifying RCTs and performed searches in MEDLINE, Embase, RCT databases, and Google Scholar from inception and up until February 3, 2025. The search, unrestricted by language, included the following terms: septic shock, RCT, dynamic measures, and fluid responsiveness. **eAppendix 1** (https://links.lww.com/CCX/B541) presents the final search strategy.

Study Selection

We used Covidence software (Veritas Health Innovation, Melbourne, Australia; available at www.covidence.org for screening articles in two stages). Two reviewers (J.W., L.B.) independently reviewed titles and abstracts and progressed citations deemed potentially eligible to the second stage for full-text review. In the second stage, we reviewed full texts of any citation deemed potentially eligible in the first stage. A third reviewer (J.B.) resolved disagreements. Non-English publications were translated using Reverso and native language speakers.

Data Extraction

Using a piloted standardized form, two reviewers extracted data independently and in duplicate. We extracted the first author, study country, number of patients enrolled, inclusion and exclusion criteria, age, intervention and control group study procedures, definition of fluid responsiveness, modality for assessing fluid responsiveness, and outcome data. Reviewers resolved disagreements by consensus or by third-party arbitration.

Data Analysis

We used RevMan (version 5.4.1; Cochrane Collaboration, Oxford, United Kingdom) software to perform random-effects meta-analysis using inverse variance for study weighting. For continuous outcomes, we converted medians into means and interquartile ranges into SDs based on guidance from the Cochrane Collaboration (9).

We present pooled continuous outcomes as mean differences (MDs) and dichotomous outcomes as risk differences (RD) and risk ratios with associated 95% CIs. We evaluated publication bias by visual inspection of the funnel plots. We also intended to use Egger's test for outcomes with more than 10 RCTs; however, we did not identify a sufficient number of RCTs to warrant this analysis. We assessed for statistical heterogeneity using visual inspection of forest plots, the chi-square test for homogeneity, and I^2 statistic. When pooled estimates exhibited important heterogeneity, we investigated potential sources by conducting subgroup analyses based on the risk of bias (high vs. low). We also intended to perform subgroup analysis based on the modality used to determine fluid responsiveness (e.g., passive leg raise vs. end-expiratory occlusion), the physiologic measure used to assess changes in cardiac output (e.g., stroke volume variation vs systolic pressure variation), and the hemodynamic assessment tool used to measure these physiologic changes (e.g., point-of-care ultrasound vs noninvasive cardiac output monitors). However, due to the limited number of studies and substantial variability in modalities across studies, we were unable to perform these additional subgroup analyses. We used the Instrument to Assess the Credibility of Effect Modification Analyses criteria to evaluate the credibility of any subgroup with an interaction p value of less than 0.05 (10).

Risk of Bias and Rating of the Evidence

We used the modified Cochrane Risk of Bias (Version 2.0) tool to assess the risk of bias in individual studies and rated the certainty of pooled outcome data using the GRADE framework (11). Following GRADE guidance, pooled data from RCTs started as high certainty evidence but were rated down if there were serious concerns with risk of bias, imprecision, inconsistency, indirectness, or publication bias. We rated our certainty based on a minimally contextualized framework. For clinical outcomes, we used an absolute effect threshold consistent with the smallest difference that patients would experience as important. For resuscitative therapies, we used the smallest difference that physicians would perceive as important. **eTable 1** (https://links.lww.com/CCX/B541) summarizes our certainty targets. Finally, we communicated results based on the GRADE narrative description (12).

RESULTS

Of 2771 citations, we reviewed 23 full-text articles and included 9 RCTs (n = 698 patients) (**eFig. 1,** https://links.lww.com/CCX/B541). Most studies enrolled participants with septic shock only (six of nine studies) (7, 8, 13–16), admitted to an ICU (seven of nine studies) (6, 13–18). **Table 1** summarizes the study characteristics.

In the control group, patients were most commonly managed using usual care as per the physician's discretion (5 of 10 studies). The passive leg raise test was the most frequently used method to increase preload in the intervention group (seven of nine studies) (6, 8, 13, 14, 16, 17, 19). The most common physiologic metric to determine fluid responsiveness was changes in stroke volume variation, with cutoffs ranging from 10% to 15% (seven of nine studies) (6, 8, 13–16, 19). We identified substantial heterogeneity in the hemodynamic monitoring used to evaluate fluid responsiveness; three studies used transpulmonary thermodilution (7, 14, 16), two studies used echocardiographic or Doppler (8, 13), two studies used bioreactance (6, 19), one study used pulse contour analysis (15), and one study did not report the hemodynamic monitoring tool used (17). **Table 2** summarizes methods to determine fluid responsiveness in the intervention groups.

We judged most studies (seven of nine studies) to be at high risk of bias due to concerns with deviations from the intended intervention (**eTable 2**, https://links.lww.com/CCX/B541). Importantly, variations in methods to increase preload, physiologic metrics, fluid responsiveness, and hemodynamic monitoring may further undermine the certainty of evidence.

Tables 3 and **4** provide the GRADE summary of findings for clinical outcomes and resuscitative therapies, respectively.

Clinical Outcomes

Using dynamic measures of fluid responsiveness probably reduce the risk of mortality at 28 days (RR 0.61; 95% CI, 0.42 to 0.90; RD –9.0%; 95% CI –18.4% to 0.0%, moderate certainty; **Fig. 1**) although with an uncertain effect on ICU mortality (RR 0.86; 95% CI, 0.56 to 1.32; RD –4.0%; 95% CI, –18.2 to 10.2, very low certainty, **eFig. 2**, https://links.lww.com/CCX/B541).

We found an uncertain effect of dynamic measures of fluid responsiveness on ICU length of stay (MD –0.38 d; 95% CI, –1.22 to 0.45; **eFig. 3**, https://links.lww.com/CCX/B541), hospital length of stay (MD –2.79 d; 95% CI, –7.44 to 1.86; **eFig. 4**, https://links.lww.com/CCX/B541), the need for MV (risk ratio 0.75; 95% CI, 0.3–1.87; RD 6.3%; 95% CI, –26.3 to 13.8; **eFig. 5**, https://links.lww.com/CCX/B541), duration of MV (MD, –2.88, 95% CI, 8.81 to 3.06; **eFig. 6**, https://links.lww.com/CCX/B541), and the need for RRT (Risk Ratio 0.68; 95% CI, 0.38 to 1.24; RD –10.2%; 95% CI –19.5 to –0.1; **eFig. 7**, https://links.lww.com/CCX/B541) (all very low certainty evidence). However, based on data from one RCT, using dynamic measures of fluid responsiveness may reduce the risk of AKI (RR 0.66; 95% CI, 0.44 to 0.98; RD –20.8%; 95% CI –39.9 to 1.7, low certainty).

Resuscitative Therapies

Using dynamic measures of fluid responsiveness may reduce the cumulative fluid balance on day 3 (MD –1.57 L; 95% CI, –2.44 L to –0.69 L, low certainty, **Fig. 2**). However, using dynamic measures of fluid responsiveness have an uncertain effect on the volume of fluid administered on day 1 post-randomization (MD –0.00 L; 95% CI, –0.65 to 0.65; **eFig. 11**, https://links.lww.com/CCX/B541), whether vasopressors were administered (RR 1.08; 95% CI, 0.83 to 1.42; RD 5.4%; 95% CI, –4.5 to 15.3; **eFig. 8**, https://links.lww.com/CCX/B541), inotrope administration (RR 0.85; 95% CI, 0.33 to 2.15; RD –0.6%; 95% CI, –5.4 to 4.2, **eFig.**

TABLE 1.
Characteristics of Eligible Studies

Study ID	Country	Study Setting	N	Age, yr, Mean (SD)	Sex, Female, *n* (%)	Population	Outcomes
Chen et al (13)	The United States	ICU	82	14.07 (0.79)	41 (50.0)	Septic shock based on Sepsis II criteria	IVF administration and cumulative fluid balance on days 3 and 5, in-hospital mortality, need for RRT, maximum vasopressor dose, duration of vasopressors, duration of MV, MAP
Cronhjort et al (14)	Sweden	ICU	34	68.35 (13.32)	15 (44.1)	Septic shock based on Sepsis II criteria	Difference in weight from day of enrollment to day 3 30-d mortality, ICU length of stay, cumulative fluid balance
Douglas et al (6)	The United States and the The United Kingdom	ICU	124	62.10 (16.24)	64 (51.6)	Sepsis or septic shock based on Sepsis II criteria	Fluid balance at 72 hr, 30-d mortality, ICU length of stay, need for RRT, need for MV, duration of MV, duration of vasopressors, change in serum creatinine, incidence of adverse events, ICU readmission, IV fluid administration at 24 hr and 72 hr, fluid balance at 72 hr, incidence of major CV endpoints, discharge location
Gruartmoner et al (17)	Spain	ICU	60	62 (15)	21 (35)	Severe sepsis or septic shock patients with tissue hypoperfusion requiring MV	28-d mortality, changes in lactate at 6 and 24 hr, and fluid balance at 72 hr
Juneja et al (15)	India	ICU	101	51.79 (11.48)	27 (26.7)	Septic shock requiring MV	Acute kidney injury, need for RRT, ICU length of stay, ICU mortality
Kuan et al (19)	Singapore	ED	122	65.45 (14.71)	51 (41.8)	Severe sepsis or septic shock, suspicion for infection, ≥ 2/4 Systemic Inflammatory Response Syndrome criteria, and serum lactate ≥ 3 mmol/L	Lactate clearance > 20% at 3 hr after start of resuscitation, in-hospital mortality, ICU mortality, 28-d mortality, need for vasoactive medications, hospital and ICU length of stay, total hospital cost
Li et al (8)	China	ED	74	63.15 (16.36)	39 (52.7)	Septic shock based on China Severe Sepsis/Septic Shock Treatment Guidelines 2014	In-hospital mortality, hospital length of stay, MAP, serum lactate, Pao_2/ Fio_2, and $ScvO_2$ 6 hr after fluid replacement therapy, CRP, and need for chest CT at 48 hr

(*Continued*)

TABLE 1. (*Continued*)
Characteristics of Eligible Studies

Study ID	Country	Study Setting	N	Age, yr, Mean (SD)	Sex, Female, *n* (%)	Population	Outcomes
Lin et al (7)	China	ICU	41	76.22 (16.12)	12 (29.3)	Septic shock (criteria not defined)	ICU mortality, 28-d mortality, duration of MV, time to achieving negative fluid balance
Richard et al (16)	France	ICU	60	64.5 (16.17)	17 (28.3)	Septic shock (Sepsis-induced hypotension despite adequate fluid resuscitation) based on Society of Critical Care Medicine/American College of Chest Physicians 1991 Criteria	Time to shock resolution, 28-d mortality, ICU length of stay, duration of MV, duration of abnormal serum lactate, pulmonary edema, organ system failure

CRP = C-reactive protein, CV = cardiovascular, ED = emergency department, MAP = mean arterial pressure, MV = mechanical ventilation, PaO_2= partial pressure of arterial oxygen, RRT = renal replacement therapy, SIRS = systemic inflammatory response syndrome.

9, https://links.lww.com/CCX/B541), and the duration of vasopressor use (MD –0.05 d; 95% CI, –0.87 to 0.77, **eFig. 10**, https://links.lww.com/CCX/B541), (all very low certainty).

Subgroup Effects

We found no evidence of credible subgroup effects based on high or low risk of bias for ICU mortality, ICU length of stay, hospital length of stay, and the provision of MV.

DISCUSSION

This systematic review provides the most comprehensive analysis of the use of dynamic measures of fluid responsiveness on outcomes in patients with sepsis and septic shock. By incorporating a structured GRADE assessment, this review provides a transparent evaluation of the strength and certainty of the evidence, filling an important gap in the existing literature. Our findings suggest that in adult patients with sepsis and septic shock, using dynamic measures of fluid responsiveness probably reduces the risk of 28-day mortality.

In addition, using dynamic measures may reduce the cumulative fluid balance by day 3 and the risk of AKI. However, their effects on ICU mortality, ICU and hospital length of stay, the need for and duration of MV, and the need for RRT remain uncertain. Likewise, the impact of vasoactive medication administration, the duration of vasopressor use, and the volume of IVF administration on day 1 is unclear.

Implications for Clinical Practice

Although the 2021 Surviving Sepsis Campaign Guidelines recommend using dynamic measures of fluid responsiveness based primarily on evidence from surgical patients (2), our findings extend this evidence to patients with sepsis and septic shock. Although we found no differences in day 1 fluid administration, which may have been influenced by variability in the timing of patient enrollment from sepsis onset, the divergence in fluid balance by day 3 suggests these measures may help clinicians recognize when additional fluids will no longer benefit patients. Using dynamic measures may spare patients the harm from excess fluid administration. When administered in excess, IVFs accumulate in the venous system, elevate CVP, and precipitate venous

TABLE 2.
Intervention and Control Group Procedures for Eligible Studies

Study ID	Control	Challenge Used for Fluid Responsiveness	Definition of Fluid Responsiveness	Cardiac Output Monitoring Tool
Chen et al (13)	Fluid management by the ICU team discretion based on available hemodynamic data	Passive leg raise, fluid bolus, or RBC transfusion	At least 2 of: pulse pressure variation decreased to < 13%, the inferior vena cava distension index decreased to < 18%, the stroke volume increase difference increased by > 10%	Transesophageal Doppler (CardioQ; Deltex Medical) and Transthoracic Doppler (ultrasonic cardiac output monitor) (CardioQ Chichester, West Sussex, United Kingdom; USCOM, Sydney, NSW, Australia)
Cronhjort et al (14)	Management based on clinician's discretion (transpulmonary thermodilution without passive leg raise test)	Passive leg raise	Stroke volume index increase ≥ 10%	Transpulmonary thermodilution (PiCCO) (Pulsion Medical Systems, Feldkirchen, Germany)
Douglas et al (6)	Management in the usual care group was according to the institution's care standards (the use of dynamic fluid assessment was prohibited)	Passive leg raise	Stroke volume increase > 10%	Bioreactance (Cheetah Medical's Noninvasive Starling SV; Cheetah Medical [Drs Sahatjian and Hansell], Wilmington, DE)
Gruartmoner et al (17)	CVP-guided fluid resuscitation according to the Survival Sepsis Campaign 2012 recommendations	Passive leg raise, pulse pressure variation, or stroke volume variation	Not reported	Not reported
Juneja et al (15)	Fluid management according to conventional indices	Stroke volume variation	Stroke volume variation (cutoff not specified)	Pulse contour analysis (Flotrac Vigelio; Edwards, Irvine, CA)
Kuan et al (19)	Usual care (administration of IV fluids, vasopressors, and inotropes as per attending physician's judgement	Passive leg raise	Stroke volume increase > 10%.	Bioreactance (Cheetah Medical's Noninvasive Starling SV; Cheetah Medical, Tel Aviv, Israel)
Li et al (8)	Traditional rapid and adequate fluid infusion regimen according to the institution's care standards	Passive leg raise	Stroke volume variation ≥ 15%	Transthoracic echocardiography (manufacturer not reported)
Lin et al (7)	Early goal-directed therapy within 6 hr of enrollment, volume status was assessed with CVP as a guide (endpoint for fluid resuscitation at CVP of 8–12 mm Hg or 10–15 mm Hg if intubated)	Fluid resuscitation guided by global end-diastolic volume index	Global end-diastolic volume index in the range of 680–800 mL/m^2	Transpulmonary thermodilution (PiCCO) (manufacturer not reported)
Richard et al (16)	Fluid bolus was given to achieve a CVP of at least 8 cm H_2O	Passive leg raise	Pulse pressure variation ≥ 13% or stroke volume increase ≥ 10% during passive leg raise	Transpulmonary thermodilution (PiCCO Plus or Intellivue MP40 monitor equipped with the PiCCO-Technology module) (Philips Healthcare, Andover, MA)

CVP = central venous pressure, PiCCO = pulse index continuous cardiac output, SV = stroke volume.

TABLE 3.
Grading of Recommendations Assessment, Development, and Evaluation Summary of Findings for the Impact of Dynamic Measures of Fluid Responsiveness-Guided Resuscitation on Clinical Outcomes

Outcome	Study Results and Measurements	Absolute Effect Estimates		Certainty of Evidence	Plain Language Summary
		Standard Care	Dynamic Measures of Fluid Responsiveness		
Mortality at 28 d	Relative Risk 0.63 (95% CI, 0.44–0.91), 499 patients (seven RCTs)	280 per 1000	176 per 1000 Difference: 103 fewer per 1000 (95% CI, 157 fewer to 25 fewer)	Low (serious risk of bias, serious inconsistency	Dynamic measures of fluid-responsiveness may reduce mortality at 28 d
ICU mortality	Relative Risk 0.86 (95% CI, 0.56–1.32), 187 patients (three RCTs)	337 per 1000	290 per 1000 Difference: 47 fewer per 1000 (from 148 fewer to 108 more)	Very low (serious risk of bias, serious inconsistency, very serious imprecision)	There is an uncertain effect on ICU mortality
ICU length of stay	425 patients (five RCTs)	4.79 d	4.93 d Difference: 0.14 d fewer (95% CI, 0.77 fewer to 0.48 more)	Very low (serious risk of bias, serious inconsistency, serious imprecision)	There is an uncertain effect on ICU length of stay
Hospital length of stay	320 patients (three RCTs)	12.63 d	15.42 d Difference: 2.79 d fewer (95% CI, −7.44 fewer to 1.86 more)	Very low (serious risk of bias, serious inconsistency, very serious imprecision)	There is an uncertain effect on hospital length of stay
Requirement for MV	246 patients (two RCTs)	216 per 1000	162 per 1000 Difference: 54 fewer per 1000 (95% CI, 151 fewer to 188 more)	Very low (serious risk of bias, serious inconsistency, very serious imprecision)	There is an uncertain effect on the need for MV
Duration of MV	102 patients (three RCTs)	7.92	5.01 Difference: 2.91 d fewer (95% CI, 8.86 fewer to 3.06 more)	Very low (serious risk of bias, serious inconsistency, very serious imprecision)	There is an uncertain effect on the duration of MV
Requirement for RRT	Relative Risk 0.68 (95% CI, 0.38–1.24), 307 patients (three RCTs)	338 per 1000	230 per 1000 Difference: 108 fewer per 1000 (95% CI, from 210 fewer to more to 81 more)	Very low (serious risk of bias, serious inconsistency, very serious imprecision)	There is an uncertain effect on the need for RRT
Acute kidney injury	Relative Risk 0.66 (95% CI, 0.44–0.98), 101 patients (one RCT)	604 per 1000	399 per 1000 Difference: 205 fewer per 1000 (95% CI, from 338 fewer to 12 fewer)	Low (serious risk of bias, serious imprecision)	Dynamic measures of fluid-responsiveness may reduce the risk of Acute kidney injury

AKI = acute kidney injury, MV = mechanical ventilation, RCT = randomized controlled trial.

TABLE 4.

Grading of Recommendations Assessment, Development, and Evaluation Summary of Findings for the Impact of Dynamic Measures of Fluid Responsiveness-Guided Resuscitation on Resuscitative Therapies

Outcome	Study Results and Measurements	Absolute Effect Estimates		Certainty of Evidence	Plain Language Summary
		Standard Care	Dynamic Measures of Fluid Responsiveness		
Vasopressor administration	Relative Risk 1.08 (95% CI, 0.83–1.42), 246 patients (two RCTs)	314 per 1000	339 per 1000 Difference: 25 more per 1000 (95% CI, 53 fewer to 132 more)	Very low (serious risk of bias, very serious imprecision)	There is an uncertain effect on whether dynamic measures of fluid responsiveness impact vasopressor administration
Inotrope administration	Relative Risk 0.85 (95% CI, 0.33–2.15), 281 patients (three RCTs)	50 per 1000	43 per 1000 Difference: 8 fewer per 1000 (95% CI, from 33 fewer to 57 more)	Very low (serious risk of bias, very serious imprecision)	There is an uncertain effect on whether dynamic measures of fluid responsiveness impact inotrope administration
Duration of vasopressors	223 patients (three RCTs)	2.55 d	2.6 d Difference: 0.05 d fewer (95% CI, 0.87 d fewer to 0.77 d more)	Very low (serious risk of bias, very serious imprecision)	There is an uncertain effect on whether dynamic measures of fluid-responsiveness impact the duration of vasopressors
Fluid administered on day 1	284 patients (three RCTs)	2.41	2.59 Difference: 0.18 L less (95% CI, 0.64 L less to 0.27 L more)	Very low (serious risk of bias, serious inconsistency, serious imprecision)	The evidence is uncertain as to whether dynamic measures of fluid-responsiveness impact hospital length of stay
Fluid balance on day 3	270 patients (four RCTs)	3.07 L	1.49 L Difference: 1.59 L less (95% CI, 2.50 L less to 0.67 L less)	Low (serious risk of bias, serious imprecision)	Dynamic measures of fluid-responsiveness may reduce the cumulative fluid balance on day 3

RCT = randomized controlled trial.

congestion (20). Venous congestion disrupts capillary blood flow through shear stress from distension, forces fluid into the interstitial space, causing organ injury, and impairs oxygen delivery by reducing the arterial-to-venous perfusion pressure gradient (21). Because fluid overload increases the risk of renal failure and mortality, dynamic measures of fluid responsiveness may be an emerging valuable tool in preventing excess fluid administration and facilitating volume removal.

Although using dynamic measures of fluid responsiveness likely reduced 28-day mortality, there remains an uncertain effect on ICU mortality. Several factors may contribute to this discrepancy. First, the limited number of studies reporting ICU mortality limits our precision around the estimate of effect. Second, various factors influence ICU mortality, including severity of illness, comorbidities, and complications developing during the ICU stay. Third, several studies included patients with sepsis and septic shock. Fourth, the mean ICU stays among included studies were shorter than 28 days, suggesting that survival benefits from fluid management strategies may manifest after ICU discharge.

Limitations

Our review has some limitations. Many studies exhibited a high risk of bias due to concerns with deviations from the intended interventions. For several

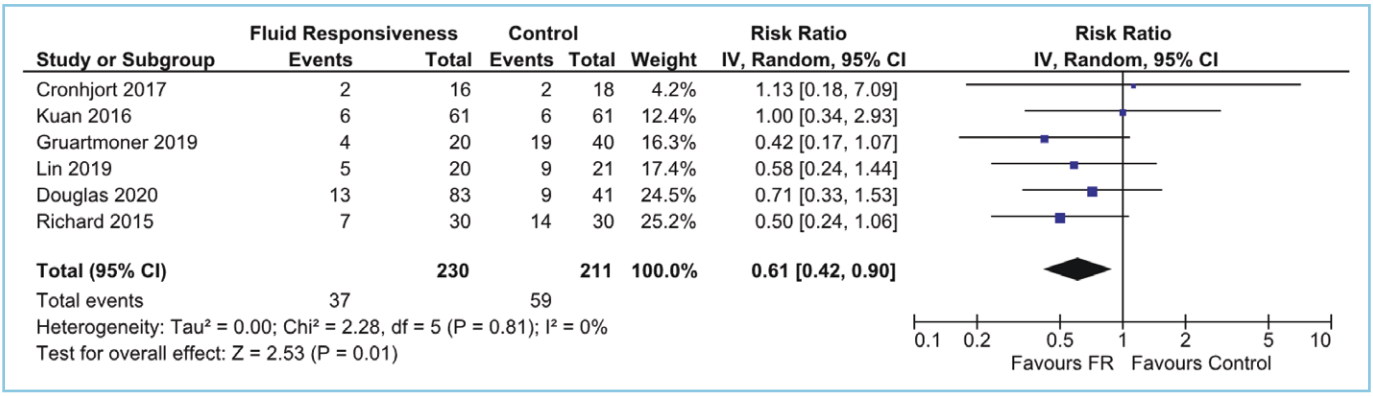
Fluid Responsiveness
Control
Risk Ratio
Risk Ratio
Study or Subgroup Events Total Events Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Cronhjort 2017 2 16 2 18 4.2% 1.13 [0.18, 7.09]
Kuan 2016 6 61 6 61 12.4% 1.00 [0.34, 2.93]
Gruartmoner 2019 4 20 19 40 16.3% 0.42 [0.17, 1.07]
Lin 2019 5 20 9 21 17.4% 0.58 [0.24, 1.44]
Douglas 2020 13 83 9 41 24.5% 0.71 [0.33, 1.53]
Richard 2015 7 30 14 30 25.2% 0.50 [0.24, 1.06]
Total (95% CI) 230 211 100.0% 0.61 [0.42, 0.90]
Total events 37 59
Heterogeneity: Tau² = 0.00; Chi² = 2.28, df = 5 (P = 0.81); I² = 0%
Test for overall effect: Z = 2.53 (P = 0.01)
0.1 0.2 0.5 1 2 5 10
Favours FR Favours Control

Figure 1. Forest plot of 28-day mortality. FR = fluid responsiveness.

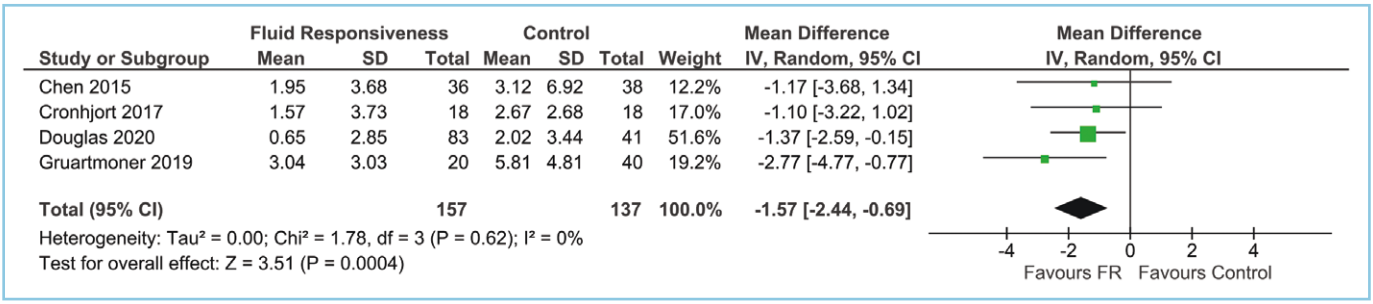
Fluid Responsiveness
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Chen 2015 1.95 3.68 36 3.12 6.92 38 12.2% -1.17 [-3.68, 1.34]
Cronhjort 2017 1.57 3.73 18 2.67 2.68 18 17.0% -1.10 [-3.22, 1.02]
Douglas 2020 0.65 2.85 83 2.02 3.44 41 51.6% -1.37 [-2.59, -0.15]
Gruartmoner 2019 3.04 3.03 20 5.81 4.81 40 19.2% -2.77 [-4.77, -0.77]
Total (95% CI) 157 137 100.0% -1.57 [-2.44, -0.69]
Heterogeneity: Tau² = 0.00; Chi² = 1.78, df = 3 (P = 0.62); I² = 0%
Test for overall effect: Z = 3.51 (P = 0.0004)
-4 -2 0 2 4
Favours FR Favours Control

Figure 2. Forest plot of cumulative fluid balance on day 3. FR = fluid responsiveness.

patient outcomes, we rated the certainty of evidence as very low due to imprecision in the estimates of effect. Varied methods for measuring preload, defining responsiveness, and monitoring hemodynamics limit the strength of our conclusions.

Due to limited data, we were unable to explore differences based on the specific methods used to determine dynamic measures of fluid responsiveness and other patient subgroups of interest. Furthermore, studies used various preload-increasing techniques (primarily passive leg raise tests) combined with different assessment approaches (pulse pressure variation, stroke volume variation) using diverse monitoring tools (arterial waveform analysis, noninvasive monitors, point-of-care ultrasound (POCUS). Furthermore, some studies relied on invasive methods requiring specialized algorithms, limiting clinical practicality. We could not separately analyze mixed populations of sepsis and septic shock patients. Finally, due to a lack of long-term data, we were unable to explore potential variability in post-resuscitation care.

Despite their value in septic shock management, dynamic measures of fluid responsiveness have important limitations. These measures identify patients whose cardiac output will increase with preload augmentation, but cannot distinguish whether this augmentation should come from volume expansion or vasopressor therapy. In septic shock, vasoplegia increases unstressed volume, decreases mean systemic filling pressure, reduces venous return, and impairs cardiac output (22, 23). Although these patients may demonstrate fluid responsiveness, vasopressor therapy may provide a more elegant physiologic solution that increases mean systemic filling pressure, mobilizes existing venous volume, and improves venous return (24).

Furthermore, although fluid responsiveness suggests patients may benefit from volume expansion, this measure does not account for the risks of fluid administration. Excess fluids may worsen venous congestion, a pathologic state where elevated CVPs impair organ perfusion through reduced venous drainage and tissue edema (21). In fact, patients who are fluid-responsive may also exhibit venous congestion (25). Furthermore, data from a large prospective observational study concluded that the decision to administer additional fluids was not always influenced by the results of fluid responsiveness, highlighting that fluid responsiveness alone is one of many factors

a clinician uses when deciding to administer fluids. Thus, although dynamic measures remain valuable tools, they alone may be insufficient to optimize the resuscitation strategy.

Future Research

Future studies should compare different measures and approaches for assessing fluid responsiveness to determine their relative effectiveness, clinical practicality, and resource utilization in various patient populations and clinical settings. We need studies that evaluate whether the use of dynamic measures of fluid responsiveness reduces mortality in patients with higher baseline sequential organ failure assessment (Sequential Organ Failure Assessment) scores, patients with exclusively septic shock, and patients with prior comorbidities that render them intolerant to fluid overload (e.g., heart failure). In addition, future research should explore the therapeutic benefits of direct interrogation of the venous system and assessment of venous congestion, as these may complement dynamic measures of fluid responsiveness to guide appropriate volume management. Other modalities, such as POCUS, can assess fluid responsiveness and may offer a pragmatic, noninvasive alternative.

CONCLUSIONS

In adult patients with sepsis and septic shock, using dynamic measures of fluid responsiveness to guide resuscitation may reduce the risk of 28-day mortality and AKI, likely through preventing excess fluid accumulation after initial resuscitation. However, the impact of this intervention on other important clinical outcomes remains uncertain. Future studies should examine more severely ill patients, compare different modalities for dynamically assessing fluid responsiveness, and incorporate venous congestion assessments to better characterize harms associated with excess fluid administration.

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